## **WEST Search History**

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DATE: Tuesday, December 06, 2005

| Hide? | Set<br>Name | Query  | <u>Hit</u><br>Count |
|-------|-------------|--|---------------------|
|       | DB=I        | PGPB, USPT, USOC, EPAB, JPAB, DWPI, TDBD; PLUR=YES; OP=OR  |                     |
|       | L1          | pyridylmethyl\$  | 10362               |
|       | L2          | pyridyl-methyl\$   | 181                 |
|       | L3          | pyridylmethylsulfinyl\$  | 93                  |
|       | L4          | pyridylmethylsulfinyl\$benzimidazo\$   | 28                  |
|       | L5          | 14 and vitamin\$   | 4                   |
|       | L6          | ascorbic or thiamine or miacin or retinol or phytonadione or riboflavin or pyridoxine or cyanocobalamin or ascorbate or cholecalciferol or nicotinic or pantothenate or folic or biotin or inositol or choline | 191749              |
|       | L7          | L6 and (13 or 14)  | 33                  |

END OF SEARCH HISTORY

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| ☐ 4. <u>20050059655</u> . 20 Aug 04. 17 Mar 05. Nitrosated and nitrosylated diuretic compounds, compositions and methods of use. Garvey, David S., et al. 514/223.2; 514/266.2 514/266.3 544/13 544/284 544/286 A61K031/549 A61K031/517 C07D285/22.  |
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Record List Display Page 3 of 3

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## Cenerate Collection Print

| Term   | Documents |
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| ((4 OR 3) AND 6).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.       | 33        |
| (L6 AND (L3 OR<br>L4)).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD. | 33        |

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PGPUB-DOCUMENT-NUMBER: 20040266828

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040266828 A1

TITLE: Nitrosated and nitrosylated proton pump inhibitors, compositions and methods of use

PUBLICATION-DATE: December 30, 2004

#### **INVENTOR-INFORMATION:**

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| Letts, L. Gordon       | Dover   | MA    | US      |
| Richardson, Stewart K. | Tolland | CT    | US      |
| Tam, Sang William      | Dover   | MA    | US      |
| Wang, Tiansheng        | Concord | MA    | US      |

## ASSIGNEE-INFORMATION:

| NAME           | CITY    | STATE | COUNTRY | TYPE CODE |
|----------------|---------|-------|---------|-----------|
| NitroMed, Inc. | Bedford | MA    | US      | 02        |

APPL-NO: 10/866303 [PALM] DATE FILED: June 14, 2004

RELATED-US-APPL-DATA: child 10866303 A1 20040614 parent division-of 09512829 20000225 US PENDING non-provisional-of-provisional 60122111 19990226 US

INT-CL: [07] <u>A61 K 31/4439</u>, <u>C07 D 43/14</u>, <u>C07 D 43/02</u>

US-CL-PUBLISHED: 514/338; 546/272.7 US-CL-CURRENT: <u>514/338</u>; <u>546/272.7</u>

DOCUMENT-IDENTIFIER: US 20040266828 A1

TITLE: Nitrosated and nitrosylated proton pump inhibitors, compositions and methods of use

## **Detail Description Paragraph:**

[0277] The compounds and compositions of the present invention can be used in this aspect of the invention with any NSAID and selective COX-2 inhibitor known in the art. Such NSAIDs include, for example, aspirin (e.g., acetylsalicylic acid), salicylate esters and salts, acetate esters of salicylic acid, diflurophenyl derivatives (e.g., diflunisal), salicylsalicylic acids (e.g., salsalate), salts of salicylic acids (e.g., sodium salicylate), salicylamide, sodium thiosalicylate, choline salicylate, magnesium salicylate, combinations of choline and magnesium salicylates, 5-aminosalicylic acid (e.g., mesalamine), salicylazosulfapyridine (e.g., sulfasalazine), methylsalicylate, and the like.

## **Detail Description Paragraph:**

[0296] The compounds and compositions of the present invention can be formulated as pharmaceutically acceptable salts. Pharmaceutically acceptable salts include, for example, alkali metal salts and addition salts of free acids or free bases. The nature of the salt is not critical, provided that it is pharmaceutically-acceptable. Suitable pharmaceutically-acceptable acid addition salts may be prepared from an inorganic acid or from an organic acid. Examples of such inorganic acids include, but are not limited to, hydrochloric, hydrobromic, hydroiodic, nitrous (nitrite salt), nitric (nitrate salt), carbonic, sulfuric, phosphoric acid, and the like. Appropriate organic acids include, but are not limited to, aliphatic, cycloaliphatic, aromatic, heterocyclic, carboxylic and sulfonic classes of organic acids, such as, for example, formic, acetic, propionic, succinic, glycolic, gluconic, lactic, malic, tartaric, citric, ascorbic, glucuronic, maleic, fumaric, pyruvic, aspartic, glutamic, benzoic, anthranilic, mesylic, salicylic, p-hydroxybenzoic, phenylacetic, mandelic, embonic (pamoic), methanesulfonic, ethanesulfonic, benzenesulfonic, pantothenic, toluenesulfonic, 2-hydroxyethanesuifonic, sulfanilic, stearic, algenic, .beta.-hydroxybutyric, cyclohexylaminosulfonic, galactaric and galacturonic acid and the like. Suitable pharmaceutically-acceptable base addition salts include, but are not limited to, metallic salts made from aluminum, calcium, lithium, magnesium, potassium, sodium and zinc or organic salts made from primary, secondary and tertiary amines, cyclic amines, N,N'-dibenzylethylenediarnine, chloroprocaine, choline, diethanolamine, ethylenediamine, meglumine (N-methylglucamine) and procaine and the like. All of these salts may be prepared by conventional means from the corresponding compound by reacting, for example, the appropriate acid or base with the compound.

## CLAIMS:

4. The compound of claim 3, wherein the benzimidazole is omeprazole, lansoprazole, pantoprazole, rabeprazole, leminoprazole, timoprazole, tenatoprazole, disulprazole, esomeprazole, 2-(2-benzimidazolyl)-pyridine, a tricyclic imidazole, a thienopydidine benzimidazole, a fluoroalkoxy substituted benzimidazole, a dialkoxy benzimidazole, a N-substituted 2-(pyridylalkenesulfinyl) benzimidazole, a cycloheptenepyridine, a 5-pyrrolyl-2-pyridylmethylsulfinyl benzimidazole, a alkylsulfinyl benzimidazole, a fluoro-pyridylmethylsulfinyl benzimidazole, an imidazo[4,5-b]pydridine, RO 18-5362 or IY 81149; wherein the quinoline is a 4-amino-3--carbonyl quinoline, a 4-amino-3-acylquinoline or a 3-butyryl-4-(2-methylphenylamino)-8-(2-hydroxyethoxy)quinoline; wherein the pyrimidine is a quinazoline, a tetrahydroisoquinolin-2-yl pyrimidine or YH 1885; wherein the thiadiazole is 3-substituted 1,2,4-thiadiazolo[4,5-a]benzimidazole or a 3-substituted imidazo[1,2-d]-thiadiazole; wherein the sulfinylnicotinamide is a 2-sulfinylnicotinamide; wherein the thienoimidazole is a pyridylsulfinylbenz imidazole, a pyridylsulfinyl thieno imidazole, a theinoimidazole-toluidine, a 4,5-dihydrooxazole, a thienoimidazole-toluidine or Hoe-73 1; wherein the imidazopyridine is a imidazo[1,2-a]pyridine, a

pyrrolo[2,3-b]pyridine or a pharmaceutically acceptable salt thereof.

DOCUMENT-IDENTIFIER: US 6962717 B1

TITLE: Pharmaceutical compositions

#### **CLAIMS:**

- 8. A composition as claimed in claim 1, wherein the active pharmaceutical ingredient is an active ingredient from the group of antidiabetics, analgesics, antiinflammatory agents, antirheumatic agents, antihypotensives, antihypertensives, psychopharmaceuticals, tranquilizers, antiemetics, muscle relaxants, glucocorticoids, agents for treating ulcerative colitis or Crohn's disease, antiallergics, antibiotics, antiepileptics, anticoagulants, antimycotics, antitussives, arteriosclerosis remedies, diuretics, enzymes, enzyme inhibitors, gout remedies, hormones and their inhibitors, cardiac glycosides, immunotherapeutics and cytokines, laxatives, lipid-lowering agents, migraine remedies, mineral preparations, otologicals, antiparkinson agents, thyroid therapeutics, spasmolytics, platelet aggregation inhibitors, vitamins, cytostatics and metastasis inhibitors, phytopharmaceuticals, chemotherapeutics and amino acids.
- 9. A composition as claimed in claim 1, wherein the active pharmaceutical ingredient is an active ingredient from the group of analgesics, agents for treating ulcerative colitis or Crohn's disease, corticosteroids, proton pump inhibitors, virus statics, lipid-lowering agents, H2 blockers, antibiotics and ACE inhibitors.
- 14. A process for producing a pharmaceutical composition as claimed in claim 1, which comprises the active pharmaceutical ingredient being mixed with a polymer insoluble in gastric and intestinal juices and compacted to a composition in such a way that the compacted composition has an average internal pore diameter, measured by mercury porosimetry at 1000 to 4000 bar, not exceeding 35 .mu.m, and comprises the compacted composition being comminuted to particles, and the particles being coated with a polymer insoluble in gastric and intestinal juices, and comprises, optionally, the coated particles being converted into a suitable dosage form.
- 15. A <u>process</u> for producing a pharmaceutical composition as claimed in claim 2, which comprises the active pharmaceutical ingredient being mixed with a polymer insoluble in gastric and intestinal juices and compacted to a composition in such a way that the compacted composition has a percent porosity not exceeding 27%, and comprises the compacted composition being comminuted to particles, and the particles being coated with a polymer insoluble in gastric and intestinal juices, and comprises, optionally, the coated particles being converted into a suitable dosage form.
- 16. A <u>process</u> as claimed in claim 14, wherein for mixing the active pharmaceutical ingredient with the polymer insoluble in gastric and intestinal juices the active ingredient is moistened with an aqueous and/or organic dispersion or solution of the polymer, and the mixture is granulated and dried.
- 17. A <u>process</u> as claimed in claim 14, wherein the compaction takes places under a pressure of at least 5 kN per cm length of press.

## **WEST Search History**

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DATE: Tuesday, December 06, 2005

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|-------|----------|---|--------------|
|       | DB=USPT; | PLUR=YES; OP=OR                             |              |
|       | L1       | 20040126318                                 | 0            |
|       | DB=PGPB; | PLUR=YES; OP=OR                             |              |
|       | L2       | 20040126318                                 | 1            |
|       | DB=PGPB, | USPT, USOC, EPAB, JPAB, DWPI, TDBD; PLUR=YE | S; $OP = OR$ |
|       | L3       | method.clm. or process.clm.                 | 2100345      |
|       | L4       | L3 and (proton near3 pump).clm.             | 295          |
|       | L5       | L4 and vitamin.clm.                         | 21           |

END OF SEARCH HISTORY

-PAT-NO: 6962717

DOCUMENT-IDENTIFIER: US 6962717 B1

TITLE: Pharmaceutical compositions

DATE-ISSUED: November 8, 2005

**INVENTOR-INFORMATION:** 

NAME

**CITY** 

STATE

ZIP CODE

**COUNTRY** 

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STATE ZIP CODE COUNTRY TYPE CODE

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03

APPL-NO: 09/890104 [PALM] DATE FILED: October 16, 2001

PCT-DATA:

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PUB-DATE 371-DATE

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PCT/IB99/00180 January 29, 1999 WO00/44353 Aug 3, 2000 Oct 16, 2001 Oct 16, 2001

INT-CL: [07] A61 K 9/14, A61 K 9/22, A61 K 9/52, A61 K 9/28, A61 K 9/46

US-CL-ISSUED: 424/490; 424/435, 424/436, 424/451, 424/458, 424/464, 424/465, 424/466, 424/467,

424/468, 424/474, 424/479, 424/489, 424/490, 424/494, 424/497

US-CL-CURRENT: <u>424/490</u>; <u>424/435</u>, <u>424/436</u>, <u>424/451</u>, <u>424/458</u>, <u>424/464</u>, <u>424/465</u>, <u>424/466</u>,

<u>424/467, 424/468, 424/474, 424/479, 424/489, 424/494, 424/497</u>

FIELD-OF-SEARCH: 424/489, 424/490, 424/464, 424/451, 424/435, 424/436, 424/458, 424/465, 424/466, 424/467, 424/468, 424/474, 424/479, 424/494, 424/497

PRIOR-ART-DISCLOSED:

### **U.S. PATENT DOCUMENTS**

#### Search Selected Search ALL Clear

|   | PAT-NO         | ISSUE-DATE     | PATENTEE-NAME             | US-CL   |
|---|----------------|----------------|---------------------------|---------|
|   | <u>4540685</u> | September 1985 | Bauer                     |         |
|   | <u>4713248</u> | December 1987  | Kjornaes et al.           |         |
|   | <u>5013727</u> | May 1991       | Halskov                   |         |
|   | <u>5178868</u> | January 1993   | Malmqvist-Granlund et al. | 424/490 |
| П | 5316774        | May 1994       | Fury et al                |         |

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### FOREIGN PATENT DOCUMENTS

| FOREIGN-PAT-NO | PUBN-DATE      | COUNTRY | CLASS |
|----------------|----------------|---------|-------|
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| 0 148 811      | July 1985      | EP      |       |
| 0 212 745      | March 1987     | EP      |       |
| 0 220 143      | April 1987     | EP      |       |
| 0 239 361      | September 1987 | EP      |       |
| 0 365 947      | May 1990       | EP      |       |
| 0 453 001      | October 1991   | EP      |       |
| 0 671 167      | September 1995 | EP      |       |
| 0 671 168      | September 1995 | EP      |       |
| 2134785        | August 1984    | GB      |       |
| WO 83/00435    | February 1983  | WO      |       |
| WO 91/18590    | December 1991  | WO      |       |
| WO 91/19483    | December 1991  | WO      |       |
| WO 92/09270    | June 1992      | WO      |       |
| WO 92/14452    | September 1992 | WO      |       |
| WO 92/16206    | October 1992   | WO      |       |
| WO 97/23199    | July 1997      | WO      |       |
| WO 97/25980    | July 1997      | WO      |       |
| WO 98/20858    | May 1998       | WO      |       |
|                |                |         |       |

**ART-UNIT: 1615** 

PRIMARY-EXAMINER: Spear; James M.

ATTY-AGENT-FIRM: Leydig, Voit & Mayer, Ltd.

#### ABSTRACT:

A pharmaceutical composition for slow release of active ingredient in the gastrointestinal tract, comprising a plurality of active ingredient-containing particles coated with a material insoluble in gastric and intestinal juices, where the particles have as core a homogeneous mixture comprising an active pharmaceutical ingredient and a polymer insoluble in gastric and intestinal juices, with an average

internal pore diameter not exceeding 35 .mu.m, makes efficient and pH-independent delaying of release possible even with comparatively small amounts of polymer. It is additionally distinguished

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L2: Entry 1 of 1 File: USPT Aug 6, 2002

DOCUMENT-IDENTIFIER: US 6428809 B1

TITLE: Metering and packaging of controlled release medication

#### Brief Summary Text (4):

The convenience of administering a single dose of a medication which releases multiple active ingredients in a controlled fashion and in a chosen location over an extended period of time, as opposed to the administration of a number of single doses at regular intervals, has long been recognized in the pharmaceutical arts. The advantage to the patient and clinician in having consistent and uniform blood levels of medication over an extended period of time are likewise recognized. The advantages of a variety of controlled-release dosage forms are well known. Among the most important advantages are: (1) increased contact time for the drug to allow for local activity in the stomach, small intestine, colon, or other locus of activity; (2) increased and more efficient absorption for drugs which have specific absorption sites; (3) the ability to reduce the number of dosages per period of time; (4) employment of less total drug; (5) minimization or elimination of local and/or systemic side effects; (6) minimization of drug accumulation associated with chronic dosing; (7) improved efficiency and safety of treatment; (8) reduced fluctuation of drug level; and (9) better patient compliance with overall disease management.

## Brief Summary Text (5):

Additionally, many experts believe controlled release drug delivery has many important non-therapeutic ramifications as well, including a financial saving to the <u>patient</u> in terms of fewer lost work days, reduced hospitalization and fewer visits to the physician.

#### Brief Summary Text (8):

As used herein "controlled-release" is used to describe a system, i.e. method and materials for making an active ingredient available to the <u>patient</u> in accordance with a preselected condition, i.e. time, site, etc.. Controlled-release includes the use of instantaneous release, delayed release and sustained release.
"Instantaneous release" refers to immediate release to the <u>patient</u>. "Delayed release" means the active ingredient is not made available until some time delay after administration. Typically, dosages are administered by oral ingestion, although other forms of administration are contemplated in accordance with the present invention. "Sustained release" refers to release of active ingredient whereby the level of active ingredient available to the <u>patient</u> is maintained at some level over a period of time. The method of effecting each type of release can be varied. For example, the active-ingredient can be placed on a semi-permeable membrane having predetermined diffusion, dissolution, erosion or breakdown characteristics.

#### Brief Summary Text (14):

Various methods have been devised to enable controlled-release systems to be delivered to a <u>patient</u> without destruction of the delivery system during manufacturing, handling and distribution. For example, controlled-release systems have been provided in the form of beads or particles which are packaged in a

gelatin capsule for oral dosage. This method of delivery of the controlled-release system prevents damage to the coating on the beads.

#### Detailed Description Text (14):

There are many drugs which could benefit from combinations to improve <u>patient</u> benefit. However, with many active ingredients, there is a question of chemical interaction. Thus, several drugs are normally prescribed as separate tablets or capsules which presents a problem in terms of <u>patient</u> compliance, e.g. TB triple therapy, AIDS multi-drug therapy, anti-infectives, etc. Also, delivery of two or more active medicaments could reduce side effects, and/or improve therapeutic response which may in turn permit a decrease in the required dosage. By way of example, we provide the following combinations:

#### Detailed Description Text (17):

(3) Enalapril.sup.5 and analogs and isomers is an ACE inhibitor used for the treatment of hypertension. This drug has been used with the following and analogs and isomers beta adrenegic-blocking agents, methyldopa, nitrate, calcium blocking agents, hydrazinc, Prazosin.sup.6 and Digoxin.sup.7 without clinically significant side effects. One or more of these agents may be combined with Enalapril to improve the compliance of patient with hypertension and hypertension and other cardiac diseases.

#### Detailed Description Text (19):

(5) Omeprazole.sup.1 and analogs and isomers is also used in combination with Clarithoromycin.sup.1 for ulcer treatment. These two drugs may be combined as a single dose for <u>patient</u> compliance.

## Detailed Description Text (20):

(6) Tamoxifen.sup.10 and analogs and isomers used in treatment of breast cancer has a+/-30% incident of water retention with weight gain >5%. This can be a disturbing consequence for <u>patients</u> with an even more disturbing disease. The addition of a diuretic or combination diuretic to form a single dosage form for reduction in side effect and compliance.

#### Detailed Description Text (22):

(8) Metformin HCl.sup.12 and analogs and isomers are hypoglycemic agents which have been used in combination with Solfonylurea.sup.13 and analogs and isomers to treat Type 2 Diabetes. These two agents act in different ways on reducing glucose levels. A combination would be helpful for those patients requiring more aggressive oral therapy for their diabetes.

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